

**REMARKS**

**I. INTRODUCTION**

Claim 25 has been amended as provided above merely to clarify the subject matter recited therein, and address the Examiner's comments. Claims 4-24, 28-36 and 44 have previously been cancelled, without prejudice. Claims 40-42 have previously been withdrawn. Applicants hereby reserve the right to pursue the cancelled and/or withdrawn claims in the above-identified application and/or one or more continuation and/or divisional applications claiming priority to the above-identified application. Accordingly, claims 1-3, 25-27, 37-39, 43 and 45-64 of the above-identified application are now under consideration.

Provided herein above, please find a claim listing indicating the amendment to claim 25, and the status of other claims on separate sheets so as to comply with the requirements set forth in 37 C.F.R. § 1.121. It is respectfully submitted that no new matter has been added. Support for the amendment to claim 25 can be found in the originally-filed application, including the specification, drawings and/or claims thereof. (See, e.g., Specification of the above-identified application, p. 13, lns. 11-15, and Figure 5).

**II. REJECTION UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN**

Claims 25-27, 45 and 55-62 stand rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. (See, e.g., Office Action, p. 3). In particular, the Examiner contends in the Office Action that the storage media recited in these claims allegedly "encompasses transitory subject matter such as a carrier

signal.” (*Id.*) The Examiner then refers to the Official Gazette notice 1351 OG 212 of February 23, 2010 entitled “Subject Matter Eligibility of Computer Readable Media” (the “Official Gazette Notice”). (*Id.*)

Applicants respectfully assert that independent claim 25, and claims 26, 27, 45 and 55-62 which depend therefrom (as previously presented) are certainly directed to statutory subject matter. Nevertheless, in the interest of expediting the prosecution of the above-identified application and address the Examiner’s comments in the Office Action, independent claim 25 has been amended herein above to recite, *inter alia*, a non-transitory storage medium.

Therefore, for at least the reasons described herein above, as well as those provided in the Official Gazette Notice, Applicants respectfully assert that the rejection of amended independent claim 25, and claims 26, 27, 45 and 55-62 which depend therefrom, under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter is now moot, and should be withdrawn.

### III. REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 1-3, 25-27, 37-39, 43 and 45-64 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Delenstarr et al., “*Estimation of the confidence limits of oligonucleotide array-based measurements of differential expression*,” Proceedings of SPIE, vol. 4266, pp. 120-131 (2001) (the “Delenstarr Publication”), in view of Z-Score, The Concise Corsini Encyclopedia of Psychology and Behavioral Science (2004) (the “Z-Score Reference”) and International Patent

Publication WO 99/49403 published September 30, 1999 by Lincoln et al. (the "Lincoln Publication"). (*Id.*, p. 4).

Applicants respectfully assert that the Delenstarr Publication, taken alone or in alleged combination with the Z-Score Reference and the Lincoln Publication fails to teach or suggest the subject matter recited in independent claims 1, 25 and 37 and the claims which depend therefrom, respectfully, for at least the reasons set forth herein below.

"To reject claims in an application under Section 103, an examiner must show an un rebutted *prima facie* case of obviousness." *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1455 (Fed. Cir. 1998). The Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966), stated:

Under Section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

Indeed, to sustain a rejection under 35 U.S.C. § 103(a), there must be some teaching, other than the instant application, to alter the prior art to arrive at the claimed invention. "The problem confronted by the inventor must be considered in determining whether it would have been obvious to combine the references in order to solve the problem." *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1998).

The objective standard for determining obviousness under 35 U.S.C. § 103, as set forth in *Graham v. John Deere, Co.*, 383 U.S. 1 (1966), requires a factual determination to ascertain: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; and (3) the differences between the claimed subject matter and

the prior art. Based on these factual inquiries, it must then be determined, as a matter of law, whether or not the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the alleged invention was made. *Graham*, 383 U.S. at 17. Courts have held that there must be some suggestion, motivation or teaching of the desirability of making the combination claimed by the applicant (the “TSM test”). See *In re Beattie*, 974 F.2d 1309, 1311-12 (Fed. Cir. 1992). This suggestion or motivation may be derived from the prior art itself, including references or disclosures that are known to be of special interest or importance in the field, or from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996).

Although the Supreme Court criticized the Federal Circuit’s application of the TSM test, see *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, (2007) the Court also indicated that the TSM test is not inconsistent with the *Graham* analysis recited in the *Graham v. John Deere* decision. *Id.*; see *In re Translogic Technology, Inc.*, No. 2006-1192, 2007 U.S. App. LEXIS 23969, \*21 (October 12, 2007). Further, the Court underscored that “it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR*, 127 S. Ct. at 1741. Under the precedent established in *KSR*, however, the presence or absence of a teaching, suggestion, or motivation to make the claimed invention is merely one factor that may be weighed during the obviousness determination. *Id.* Accordingly, the TSM test should be applied from the perspective of a person of ordinary skill in the art and not the patentee, but that person is creative and not an automaton, constrained by a rigid framework. *Id.* at 1742.

However, "the reference[s] must be viewed without the benefit of hindsight afforded to the disclosure." *In re Paulsen*, 30 F.3d 1475, 1482 (Fed. Cir. 1994).

The prior art cited in an obviousness determination should create a reasonable expectation, but not an absolute prediction, of success in producing the claimed invention. *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988). Both the suggestion and the expectation of success must be in the prior art, not in applicant's disclosure. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1207 (Fed. Cir. 1991) (citing *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988)). Further, the implicit and inherent teachings of a prior art reference may be considered under a Section 103 analysis. See *In re Napier*, 55 F.3d 610, 613 (Fed. Cir. 1995).

Secondary considerations such as commercial success, long-felt but unsolved needs, failure of others, and unexpected results, if present, can also be considered. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-39 (Fed. Cir. 1983). Although these factors can be considered, they do not control the obviousness conclusion. *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988).

Absence of a property which a claimed invention would have been expected to possess based on the teachings of the prior art is evidence of nonobviousness. *Ex parte Mead Johnson & Co.* 227 USPQ 78 (Bd. Pat. App. & Inter. 1985). Evidence of unobvious or unexpected advantageous properties can rebut *prima facie* obviousness. *In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987).

To establish obviousness, the prior art references must be evaluated as a whole for what they fairly teach and neither the references' general nor specific teachings may be ignored. *Application of Lundsford*, 357 F.2d 385, 389-90 (CCPA

1966). A reference must be considered for all that it teaches, not just what purportedly points toward the invention but also that which teaches away from the invention.

*Ashland Oil, Inc. v. Delta Resins & Refractories*, 776 F.2d. 281, 296 (Fed. Cir. 1985).

Independent claims 1, 25 and 37 recite, *inter alia*, process, non-transitory storage medium and system, respectively, at least one interval associated with a dataset is determined, **the determination of a plurality of subintervals of the at least one interval is performed by repeatedly dividing the at least one interval until at least one predetermined criteria is met**, and the determination of statistically-outlying data points present in the at least one dataset is performed based on information related to the subintervals, where each particular data point of the statistically-outlying data points is (i) associated with a particular interval of the subintervals, and (ii) determined as a function of a length of the particular subinterval of the subintervals associated with the particular data point.

The Delenstarr Publication relates to, e.g., “[e]stimation of the confidence limits of oligonucleotide microarray-based measurements of differential expression.” (*Delenstarr Publication*, Title). In particular, this publication describes a method that “used a combination of fluor-exchanged two-color labeling and improved normalization methods to minimize systematic errors from labeling bias, imperfect features, and mismatched sample concentrations.” (*Id.*, Abstract). According to the Delenstarr Publication, “[o]n-microarray specificity control probes and experimentally proven probe design algorithms were used to correct for cross-hybridization.” (*Id.*) “Random errors were reduced via automated non-uniform feature flagging and an advanced scanner design.” (*Id.*) “[F]eature significance [was scored] using established statistical tests.”

(*Id.*) “[T]he intrinsic random measurement error [was then estimated] as a function of average probe signal via sample self-comparison experiments (human K-562 cell mRNA).” (*Id.*)

The Z-Score Reference provides an encyclopedia definition of Z-Score. For example, the Z-Score Reference describes that “[t]he z-score, also known as the standard score, is the result of a transformation of raw data, and this conversion can be summed up as follows: Something minus its mean divided by its standard deviation.” (*Z-Score Reference*, first paragraph).

The Lincoln Publication “relates generally to bioinformatics, and particularly to a system and method for analyzing bimolecular sequences.” (*Lincoln Publication*, p.1, lns. 6-7).

Applicants respectfully assert that the Delenstarr Publication does not at all teach, suggest or disclose any process, storage medium or system using which the determination of a plurality of subintervals is performed by repeatedly dividing an interval until a criteria is met, much less that the determination of statistically-outlying data points present in the dataset is performed based on information related to the subintervals, much less still where each of the statistically-outlying data points is associated with a particular subinterval, and determined as a function of the length of such subinterval, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application.

In the Office Action, the Examiner alleges that “[t]he abscissa axes of Figure 1b of Delenstarr et al. illustrate the intervals associated with each of the red and green channels [and that t]his interval is broken down into subintervals in the form of

widths of histogram bars.” (Office Action, pp. 5-6). The Examiner then contends that “[i]n other words, the intervals of Figure 1b of Delenstarr et al. are divided into subintervals until the criterion of the entire histogram being displayed with the bars of the given width is met.” (*Id.*, p. 6). The Examiner further purports that “[t]he data within the histograms are considered to be outlying data if the histogram bar is more than two standard deviations away on either side on (sic) the mean” and relies on “the last full paragraph of page 121” of this publication in alleged support of this contention. (*Id.*) The Examiner then believes that “in determining whether a histogram bar corresponds to an outlier, the data point is associated with the subinterval that encompasses it, which, in turn, is determined as a function of length from the mean (in this instance, length is the number of standard deviations from the mean).” (*Id.*)

However, Applicants respectfully assert that the Examiner’s interpretation of the Delenstarr Publication is flawed and nonsensical, and that the Delenstarr Publication certainly does not even teach or suggest the subject matter based on such flawed interpretation. As described in the Delenstarr Publication, “[t]he example in Figure 1b [thereof] shows pixel histograms from both the green and red channels of a feature.” (Delenstarr Publication, p. 121, section 3.1.1). “This example used the mean  $\pm 2$  standard deviations (SD) of the population as the range for inlier pixels.” (*Id.*) “Those pixels outside of this range are deemed outliers and are removed from further calculations.” (*Id.*) “A new mean and standard deviation are then calculated for each feature, using only the inlier pixels.” (*Id.*) “This process is performed for each feature and each feature’s local background region, in both the green and red channels.” (*Id.*)



First, Applicants respectfully assert that each of the pixel histograms from both the green channels and the red channels of a feature (that is illustrated in Figure 1b of the Delenstarr Publication) is certainly not (and cannot be) equivalent to the interval as recited in independent claims 1, 25 and 27 of the above-identified application, as such purported correspondence would not make sense.

Second, even if, assuming *arguendo*, these histograms are interpreted as being equivalent to the recited interval (with which interpretation Applicants disagree), the widths of histogram bars of the Delenstarr Publication are certainly not equivalent to the sub-intervals as recited in independent claims 1, 25 and 27. Rather, as described in the Delenstarr Publication, Figure 1b of the Delenstarr Publication indicates two separate histograms of signals, i.e., one for the Green channel, and one for the Red channel representing pixels. (See, e.g., Delenstarr Publication, Figure 1b).

Third, contrary to the Examiner's contention, neither the histograms nor the histogram bars of the Delenstarr Publication are repeatedly divided until a criteria is met in a determination of a plurality of subintervals, which is required in independent claims 1, 25 and 27. Indeed, the Delenstarr Publication does not teach or suggest **repeatedly dividing an interval at all**. Rather, as described in the Delenstarr Publication, "pixels outside of [the mean  $\pm$  2 standard deviations] range are deemed outliers and are removed [and a] new mean and standard deviation are then calculated for each feature." (*Id.*, p. 121, section 3.1.1). Thus, no "subdivision" occurs in the Delenstarr Publication whatsoever. Applicants respectfully assert that one having ordinary skill in the art would have understood that removing the histogram bars representing outliers ( $> 2$  standard deviations from the mean) before performing further

calculations is certainly not any **division of an interval**, much less a repeated division, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application.

Fourth, Applicants respectfully assert that the Examiner's contention in the Office Action that the "length [**of a particular subinterval**] is the number of standard deviations from the mean" is *nonsensical, and counter to the Examiner's further contention in the same paragraph* of the Office Action that the widths of the histogram bars are allegedly equivalent to the recited subintervals and that "histograms are considered to be outlying data if the histogram bar is more than two standard deviations away on either side of the mean." (Office Action, p. 6). Indeed, **it is not possible for a histogram bar to be more than two standard deviations away from the mean if the width of the histogram bar is equivalent to a subinterval having a length equal to the number of standard deviations from the mean**, as purported by the Examiner on pages 5 and 6 of the Office Action.

Thus, Applicants respectfully assert that the Delenstarr Publication certainly does not teach or suggest any process, storage medium or system using which the determination of a plurality of subintervals is performed by repeatedly dividing an interval until a criteria is met, much less that the determination of statistically-outlying data points present in the dataset is performed based on information related to the subintervals, much less still where each of the statistically-outlying data points is associated with a particular subinterval, and determined as a function of the length of such subinterval, as explicitly recited in independent claims 1, 25 and 37 of the above-identified application.

It is further respectfully asserted that the Z-Score Reference and the Lincoln Publication fail to cure at least the deficiencies of the Delenstarr Publication that are described herein above, and the Examiner does not assert that these publications do.

Therefore, for at least the reasons provided herein above, the rejection of independent claims 1, 25 and 37, claims 2, 3, 43 and 47-54 which depend from independent claim 1, claims 26, 27, 45 and 55-62 which depend from amended independent claim 25, and claims 38, 39, 46, 63 and 64 which depend from independent claim 37, under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Delenstarr Publication, in view of the Z-Score Reference and the Lincoln Publication, should be withdrawn.

IV. CONCLUSION

In light of the foregoing, Applicants respectfully submit that all claims under consideration 1-3, 25-27, 37-39, 43 and 45-64 and are in condition for allowance. Prompt consideration, reconsideration and allowance of all of the claims of the above-identified application are therefore earnestly solicited. If any issues remain outstanding, the Examiner is invited to contact the undersigned via the telephone number provided below.

Respectfully submitted,

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